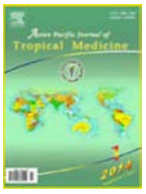
Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Medicine

journal homepage:www.elsevier.com/locate/apjtm



Document heading doi: 10.1016/S1995-7645(14)60257-1

Ethnobotanical study of medicinal plants used in the management of diabetes mellitus in the Urmia, Northwest Iran

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ARTICLE INFO

Article history:
Received 3 Jul 2014
Received in revised form 25 Aug 2014
Accepted 31 Aug 2014
Available online 29 Sep 2014

Keywords:
Ethnomedicine
Diabetes
Urmia
Iran

ABSTRACT

Objective: To collect and document information on anti-diabetic plants traditionally used in the treating of diabetes in Urmia at Northwest Iran because ethnomedicines are considered as valuable sources to find new potential drugs.

Methods: We used the method of direct observation and interview (35 traditional healers) along with gathering herbarium specimens mentioned plants in site.

Results: There were 30 medicinal plants from 17 families for the treatment of diabetes. The family with most plants was Lamiaceae (20%). Leaves (20%) are often used and its form is decoction (70%). It was also found that *Citrullus colocynthis* has the most frequency of use among traditional healers.

Conclusions: Furthermore, base on current findings many of the mentioned plants have potential active ingredients to influence diabetes.

1. Introduction

Diabetes mellitus is one of the most prevalent diseases in endocrine gland system with an increasing incidence in human community[1]. Type I diabetes is caused by insulin secretion deficit while type II diabetes is accompanied with progressive rate of insulin resistance in liver and peripheral tissues, reducing β-cells mass, and deficient insulin secretion[2,3]. This disease brings about acute metabolic side effects including ketoacidosis, hyperosmolar coma accompanied with chronic disorders and long term, adverse side effects such as retinopathy, renal failure, neuropathy, skin complications, as well as increasing cardiovascular complication risks[4,5]. Also, common symptoms of diabetes are frequent urine, thirsty, and overeating[6].

Diabetes inflicts 100 million people yearly and is recognized as the seventh cause of death in the world[7]. It has been estimated that the number of diabetic people will increase from 150 million individuals in 2003 to 300 million by 2025[8].

The essential and effective drugs for diabetes mellitus are insulin injection and hypoglycemic agents, but these compounds possess several adverse effects and have no effects on diabetes complications in long term. Regarding the human increased knowledge about this disease and its complications, it is necessary to find effective compounds with lower side effects in treating diabetes[9]. Medicinal plants are good sources as alternative or complementary treatments for this and other diseases[10-12].

Although various plants have been traditionally used throughout history to reduce blood glucose and improve diabetes complications, there is not enough scientific information about some of them. Herbal medicines are

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Foundation Project: Supported by the Deputy for Research and Technology of Lorestan University of Medical Sciences (Grant No. 0207).

commonly prescribed throughout the world because of low side effects, availability, roughly low cost, and also its effectiveness[13,14].

In the present situation, herbal medicines' usage has significantly increased and published studies from developed countries emphasize that a paramount proportion of medicines supplied by them have herbal origins, so growing and producing the herbal medicines could be helpful to both economic development and community's health[15,16]. World Health Organization has announced that 80% of people around the world use herbal medicines at initial level of health remedy in the same way and they need to be evaluated scientifically for their efficacies[17].

The plants as a major source of food supplements are effective in controlling blood glucose and preventing long term complications in type II diabetes[18]. The positive effects of many herbal medicines in reducing blood glucose and its complications have been already recognized[19-21].

Iran as an old civilized country has a valuable traditional system of medicine called traditional Persian medicine and rooted in thousands years ago[22-25]. During early medieval age, Persian physicians such as Akhawayni, Rhazes, Avicenna, Haly Abbas, Jorjani, *etc*. have flourished medical sciences while some of their manuscripts like Canon of Medicine were added in main textbooks in eastern and western universities until 18th century[26-30]. Regarding, current ethno-medicine in Iran with such great background it is popular among people and is a potentially good source for finding new natural remedies. Twenty-three Persian physicians knew and diagnosed diabetes for centuries and had potentially good medicines (based on current knowledge) to manage and treat it[31].

Urmia, a big city in Northwest Iran, is one of the places that ethno-medicine is popular and has good mountain weather to growth medicinal plants. In this study, we tried to obtain and analyze ethno pharmacological data of medicinal plants used to control and treatment of diabetes mellitus by traditional healers.

2. Methods

2.1. Study area

Forest landscape of Darre Ghasemloo and its adjacent regions with an area of 57 700 km^2 is located in southern part of Urmia City in Iran. It covers 45° 5′ to 45° 10′ E and 37° 15′ to 37° 20′ N geographical coordinates. It is located in 30 km right part of Urmia-Oshnaviyeh Road. This region is mountainous with the lowest altitude of 1 420 m and the highest altitude of 2 280 m[32]. With regard to the meteorological information of region and annual humidity condition of soils, the soil moisture in this area under study were xeric and mesic, respectively[33]. According to climatic divisions, this region is cold and semi-arid. The mean annual rain fall is 367.5 mm, the highest and the lowest annual mean temperature is 33.1 °C and −15.5 °C, respectively. In this area, February and August are the coldest and the warmest months of year, respectively[34].

2.2. Method of collecting data

This study was conducted via questionnaire and interview during November, 2013 to December, 2013 by traditional healers who are considered as unwritten knowledge.

Firstly, a full list of Urmia county herbalists (traditional healers) was obtained from Food and Medicine Assistance Department of Urmia University of Medical Sciences. Observation and interview accompanied (face to face) by gathering herbarium specimens of medicinal herbs and typical and effective impacts in treating diabetes were used. The questionnaires consisted of personal information and a list of native plants' names, the used organ parts, its usage, and traditional remedy effect.

There are 47 traditional healers in Urmia that only 35 of them cooperate with us. They announced that they referred to people with diabetes who had been diagnosed with a blood test lab.

The herbarium specimens obtained based on the native herbalists' information were collected from study area. The herbarium samples obtained from data of local traditional physicians in the questionnaire were collected from the region and then they were authenticated by a botanist (Mortaza Rafieian). A herbarium specimen from each plant (whole or the used part) was prepared and deposited in the herbarium unit of Shahrekord University of Medical Sciences. Finally, the data were analyzed using Excel 2010 software.

Prepared ethno-medicinal plants were listed and compared with current knowledge about them. Also, the frequency of ethno-medicinal use in Urmia was calculated via data mentioned by traditional healers (as a percentage among 35 healers). Finally, it is tried to present potential medicinal herbs for diabetes mellitus treatment via these data.

3. Results

Thirty medicinal plants from 17 families for diabetes treatment were identified. The families with most antidiabetic plants included Lamiaceae (6%), Fabaceae (4%),

and Rosaceae (4%) (Figure 1).

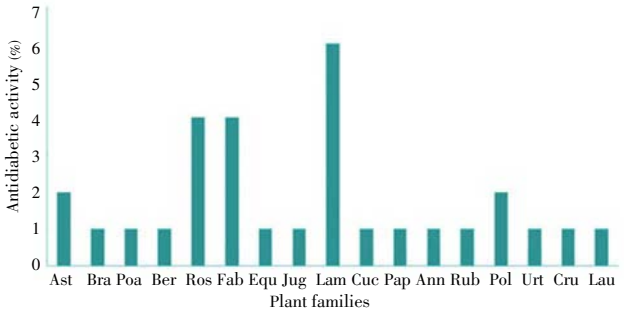

Figure 1. The families and percentage of plants with antidiabetic activity included.

Ast: Asteraceae; Bra: Brassicaceae; Poa: Poaceae; Ber: Berberidaceae; Ros: Rosaceae; Fab: Fabaceae; Equ: Equisetaceae; Jug: Juglandaceae; Lam: Lamiaceae; Cuc: Cucurbitaceae; Pap: Papaveraceae; Ann: Anacardiaceae; Rub: Rubiaceae; Pol: Polygonaceae; Urt: Urticaceae; Cru: Cruciferae; Lau: Lauraceae.

Leaves (20%) were frequently used and its form was decoction (70%). It was also found that *Citrullus colocynthis* (*C. colocynthis*) is frequently used by traditional healers.

The most used organ parts are shown in Figure 2. As it is illustrated in Figure 2, the most used organ parts in diabetes remedy in present study was 20% leaf, 16% flowering shoot, 13% fruit, 11% crust stem and 11% seed. Urmia traditional healers prescribed 70% of antidiabetic herbal medicines in the decoction forms (Figure 3). The percentage of different used organ parts and of used type are indicated in Figures 2 and 3, respectively.

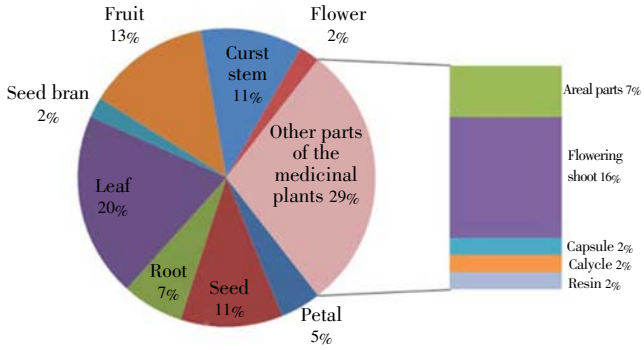

Figure 2. The percentage of different organ parts used.

The list and information of ethnobotanical remedies for diabetes treatment mentioned by Urmia, traditional healers are presented in Table 1. It shows that *C. colocynthis*, *U. dioica*, *L. album*, *Rosa foetida*, *Sanguisorba minor*, *Sophora alopecuroides*, *Trifolium pratense*, *Salvia nemorosa*, *Teucrium orientale*, *T. polium* were the most commonly used species for management of diabetes (frequency of use) by traditional healers.

Table 1

Ethnobotanical remedies for the treatment of diabetes.

Scientific name	Family	English name	Curative effect	Biological form	Growth form	Used part	Frequency of use*	Way of using
Achillea millefolium L.	Asteraceae	Milfoil	Antidiabetic	He	Herbaceous perennial	Inflorescence	9 (25.71%)	Boiled, steamed
Alyssum desertorum Stapf.	Brassicaceae	Hedge mustards	Antidiabetic	Th	Herbaceous annuals	Seed	10 (28.57%)	Boiled, herbal fumigation
Arctium lappa L.	Asteraceae	Burdock	Antidiabetic	He	Two-year herbaceous	Root, leaf	8 (22.85%)	Boiled, steamed
Avena sativa L.	Poaceae	Oat	Blood refining	Th	Herbaceous annuals	Seed, glumelle	10 (28.57%)	Boiled
Berberis integerima Bunge.	Berberidaceae	Barberry	Antidiabetic	Ph	Shrub	Fruit, leaf, skin	10 (28.57%)	Boiled, steamed
Cerasus microcarpa	Rosaceae	Sour cherry	Blood refining	Ph	A bushes	Fruit	10 (28.57%)	Boiled, raw use
Cinnamomum verum	Lauraceae	Cinnamon	Antidiabetic	Th	Herbaceous perennial	Skin	8 (22.85%)	Boiled
C. colocynthis (L.) Schrad.	Cucurbitaceae	(Common caper-bush) Colocynthis	Antidiabetic		Herbaceous annuals	Fruit	28 (80%)	Boiled
Coronilla varia L.	Fabaceae	Garden alfalfa	Antidiabetic	He	Herbaceous perennial	Leaf	8 (22.85%)	Raw use, boiled
Crataegus aronia (L.) Bosc ex Dc.	Rosaceae	Hawthorn	Antidiabetic	Ph	Shrub	Fruit and skin	9 (25.71%)	Raw use, boiled
Crataegus oxycantha L.	Rosaceae	Hawthorn	Antidiabetic	Ph	Shrub	Fruit, flower root, skin	9 (25.71%)	Raw use, boiled
Equisetum arvense L.	Equisetaceae	Horse pipe	Antidiabetic	Cr	Herbaceous perennial	Aeration organ	9 (25.71%)	Boiled
Juglans regia	Juglandaceae	Walnut tree	Antidiabetic	Ph	Arboreal	Fruit, leaf and skin	9 (25.71%)	Boiled
L. album L.	Lamiaceae	White nettle	Antidiabetic	Th	Herbaceous annuals	Flowering offshoot	25 (71.42%)	Boiled
Nasturtium officinalis (L.) R. Br.	Cruciferae	Water cress	Antidiabetic	He	Herbaceous perennial	Leaf, root	8 (22.85%)	Boiled
Nepeta bracteata Benth.	Lamiaceae	Horsemint	Antidiabetic	Th	Herbaceous annuals	Flowering offshoot	8 (22.85%)	Boiled, steamed
Nepeta meyeri Benth.	Lamiaceae	Horsemint	Antidiabetic	Th	Herbaceous annuals	Flowering offshoot	8 (22.85%)	Boiled, steamed
Papaver rhoeas L.	Papaveraceae	Copse	Antidiabetic	Th	Herbaceous annuals	Seed, capsule	8 (22.85%)	Boiled
Polygonum aviculare L.	Polygonaceae	Polygonum	Antidiabetic	Th	Herbaceous annuals	Aeration organ	8 (22.85%)	Boiled
Rhus coriaria L.	Anacardiaceae	Sumach	Blood refining	Ph	Arboreal	Fruit, leaf, resin	8 (22.85%)	Boiled
Rosa foetida Hermam.	Rubiaceae	Yellow eglantine	Antidiabetic	Ph	A bushes	Petal	25 (71.42%)	Boiled
Rumex sculantus L.	Polygonaceae	Sorrel	Blood refining	He	Herbaceous perennial	Fruit, leaf	9 (25.71%)	Raw use, boiled
Salvia nemorosa L.	Lamiaceae	Farm sage	Antidiabetic	He	Herbaceous perennial	Flowering offshoot	22 (62.85%)	Boiled
Sanguisorba minor Scop.	Rosaceae	Poterium	Antidiabetic	He	Herbaceous perennial	Fruit, leaf	24 (68.57%)	Raw use, boiled
Sophora alopecuroides	Fabaceae	Pagoda tree	Antidiabetic	He	Herbaceous perennial	Inflorescence	24 (68.57%)	Boiled
Teucrium orientale L.	Lamiaceae	Germander	Antidiabetic	He	Herbaceous perennial	Leaf	22 (62.85%)	Boiled
T. polium L.	Lamiaceae	Germander	Antidiabetic	He	Herbaceous perennial	Flowering offshoot	22 (62.85%)	Boiled
Trifolium pratense L.	Fabaceae	Clover	Antidiabetic	He	Herbaceous perennial	Flowering offshoot	22 (62.85%)	Boiled
Trifolium purpureum Loisel.	Fabaceae	Clover	Antidiabetic	He	Herbaceous perennial	Flowering offshoot	11 (31.42%)	Boiled
U. dioica L.	Urticaceae	Nettle	Antidiabetic	He	Herbaceous perennial	Seed, aeration organ	25 (71.42%)	Boiled

*: Calculated by 35 healers, n(%); *Lamium album* L.: *L. album*; *Teucrium polium* L.: *T. polium*; *Urtica dioica*: *U. dioica*.

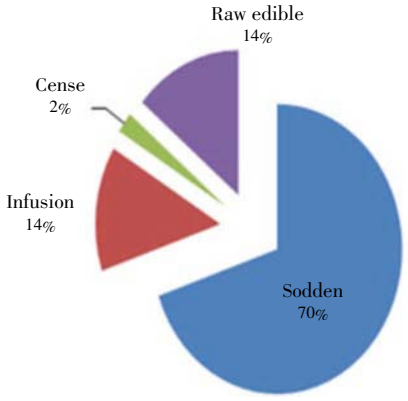

Figure 3. The percentage of type used.

4. Discussion

Current findings show many using medicinal herbs by Urmia traditional healers have antidiabetic effects. *C. colocynthis* could be applied in controlling blood glucose increment[35]. Colocynthis fruits have been prescribed in order to reduce blood glucose in traditional systems of medicine of many countries[36]. *In-vivo* studies show colocynthis juice can lead to reducing blood glucose[37]. An experimental study indicates that *U. dioica* possesses glucose reduction effect[38]. The fractions of nettle (*U. dioica*) cause an increase in insulin secretion in Langerhans Island taken from hyperglycemic mouse[39]. *U. dioica* and *L. album* can enhance insulin secretion in Langerhans Island and cause antidiabetic and blood glucose-reducing effects[39]. Current findings also showed that anti-diabetic property of nettle was due to its α-glycosidase inhibitor effect[40]. Furthermore, flavonoids can be effective in improving the blood glucose indexes via their antioxidant activity[41]. Regarding, hydro alcoholic extraction of nettle could lead to rebuild β-cells in pancreas via its antioxidant characteristics. On the other hand, tannin and carotenoids, as nettle's constituents could be effective in improving blood glucose indexes[42].

The fruit of a kind of dog rose (*Rosa canina* L.) is conventionally used in order to prevent and treat sweet diabetes[43].

Investigations show barberry could lead to induce glucose uptake in a time- and dose-dependent manner. Several inhibitors indicated that this effect was not through insulin signaling but by means of adenosine monophosphate-activated protein kinase, which its downstream molecule is P38 mitogen-activated protein kinase[44].

Burdock contains inulin. In a study, sugar was not obviously seen in diabetes-afflicted people's urine who took 120 g inulin daily[45,46]. Taking inulin led to reduce the risk of cardiovascular disease because of triglycerides synthesis and fatty acids in liver. Nowadays, inulin is used successfully because of enjoying lower calorie content, food fiber enrichment, and other nutritional characteristics[47].

A kind of *Salvia officinalis* has glucose reducing effect[48]. Some investigations confirmed that *Salvia officinalis* could showed hypoglycemic and antidiabetic feature[49,50].

In herbal medicine, walnut is considered as a plant effective in treating diabetes[51]. The compounds of walnut tree leaves like phenolic acids and flavonoids (including querectin, galactoside, querectin pentoxide derivatives, querectin arabinoside, querctin glysolid, and querectin rhamnoside) inhibit *in vitro* human plasma and low density lipoprotein oxidation[52,53]. Generally, flavonoids can lead to glucose plasma decline[54]; therefore, walnut antidiabetic quality may be due to the flavonoids involved.

Flavonoids are as key compounds for treating and managing diabetes in plants, vegetables, and fruits. Flavonoids, such as querectin, cause insulin secretion and are also considered as a strong inhibitor in sorbitol accumulation throughout the body[55,56]. It may be the reason for positive effect of traditional herbal medicines effective in treating diabetes. The useful effect of flavonoids could be the result of increasing inter-cellular antioxidants levels, preventing capillaries rupture, and boosting the body immune system, all of which are totally effective in diabetes improvement[57,58]. Taking 1-2 g flavonoids mixture is helpful to cure diabetes disease and its complications[59].

Mulberry plant reduces blood glucose due to enhancing glucose peripheral re-absorption[60]. Antidiabetic activities of mentioned plants may also have been attributed to the following components. Barberry owns some effective substances such as chelidonic acid, resin, tannin, citric acid, and malic acid. Watercress contains gluconasturtiin. Milfoil has achillin. Sorrel dock owns oxalate salts. Copse includes *Papaver* and resins and also clover (trifolium) has phytosterogen[61].

Abrus precatorius includes trigonelline which is a phytohormone and reduce blood glucose through its inhibitory effect on glucose-6-phosphatase and glycogen phosphorylase[62]. Trigonelline leads to enhance insulin receiver contents in blood red globules, hence improving glucose uptake in body tissues. Alleviating glucose level and inhibitory effect on two main enzymes of glucose metabolism by trigonelline could be promising for producing new medicines in treating diabetes[63].

In Arasbaran area (northwest of Iran), *Equisetum arvense* L. and *Rubus caesius* L. are used as antidiabetic drugs[64]. In the traditional medicine of Shiraz (Southern Iran), plants *Glaucium oxylobum* Boiss and Buhse, *Glaucium grandiflorum* Boiss and Huet, *L. album* Ky. ex Boiss., *Scorzonera canada* (*C.A.Mey.*) *O. Hoffm.*, *T. polium* and *Solanum nigrum* are the antidiabetic herbs[65,66]. Plants in Kerman Province, located in east of Iran, *Coriandrum sativum*, *Hordeum vulgare* and *Peganum harmala* are antidiabetic herbs in that region[67]. In Isfahan (Central Iran), plants such as *Juglans regia* L., *Hordeum vulgare* L., *Cucurbita pepo*, *Coriandrum sativum* L. and *Mentha spicata* L. are used as antidiabetic plant sources[68]. In Ilam Province

(west of Iran), plants such as *C. colocynthis* L., *Glycyrrhiza glabra* L., *Gundelia tournefortii* L. and *Myrtus communis* L. are used in antidiabetic medicine in this region[69]. Comparison of the antidiabetic plants in Ghasemloo Valley with other parts of Iran shows that many plants are indigenous which has been reported for the first time.

Currently, there is no data on herbal plants used to treat diabetes in northwest of Iran. Therefore, these findings are so important in the management of diabetes and future study on traditional medicine in drug development.

It is important to find curative medicines effective in treating diabetes and also disease improving drugs with lower side effects. Many studies have been carried out about herbal medicines and plants' effective substances could be applicable to diabetes remedy. One of the most significant research scopes is to exam the disease changing effect, *i.e.* the efficiency of herbal medicines in preventing diabetes progress, which requires doing experiments on mechanisms, herbal medicines efficiency and safety as well as useful potential botanical substances in diabetes disease remedy.

It should be noted that diabetes mellitus is accompanied with severe increases in oxidative stress[70-73]. Oxidative stress, other than diabetes, is also involved in a lot of curable hard diseases such as atherosclerosis[74,75], cardiovascular diseases[76,21], cancer[55,77], Alzheimer[78], gastrointestinal[79,80] and infectious diseases[81,82]. Most of medicinal plants possess antioxidant activity[83,84], thanks to polyphenolic compounds such as flavonoids, flavonols and anthocyanins which have been seen in a lot of medicinal plants reported in this paper[83,85,86]. Medicinal plants with antioxidant activity have been able to counteract with the development of these complications. The antioxidants usually scavenge the free radicals which cause oxidative stress[73,87]. Therefore, plants' effectiveness in diabetes mellitus should counteract, at least in part, with oxidative stress induced through diabetes, reducing its symptoms.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

The authors appreciate scientific supports of Urmia University of Medical Sciences and Shahrekord University of Medical Sciences. This research was supported by the Deputy for Research and Technology of Lorestan University of Medical Sciences (Grant No. 0207).

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